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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,708	09/29/2003	Harry A. Dugger III	009102-999029	9259

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EXAMINER

HAGHIGHATIAN, MINA

ART UNIT PAPER NUMBER

1616

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/671,708

Applicant(s)

DUGGER ET AL.

Examiner

Mina Haghighatian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) 1-12,30-49 and 51-74 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-29,50 and 59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>09/03 & 07/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Claims 1-12, 30-47 and 66-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 03/03/06.

Claims 48-49, 51-58 and 59-65 are withdrawn from examination at this time as being drawn to a nonelected **SPECIES**. The elected species, stimulating erythropoiesis is examined in claims 50 and 59.

Note: certain concentration ranges in the claims, such as "0.1 and 99.8", "1 and 95", "5 and 75", "0.5 and 4", etc, do not correspond to concentration ranges stated in the specification. It is the Applicant's responsibility to examine all concentration ranges stated in the claims and assure they correspond to the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deihl (WO 9413280) in view of Fassberg et al (EP 0656206A1) and further in view of Kanios et al (5,719,197) or alternatively in view of Physicians' Desk Reference, 1995.

Deihl teaches a **sprayable analgesic** composition comprising an analgesic compound which is absorbed into the bloodstream through the **buccal mucosa** and a pharmacologically acceptable liquid carrier. In a preferred embodiment the active agent is ibuprofen and the liquid carrier is **aqueous ethanol** (see page 3). The formulation may also contain other ingredients such as surfactants, humectants, **flavoring agents**, etc (see page 4). The table in example I shows the concentration ranges of each ingredient. Deihl fails to disclose other suitable active agents for the said formulation, or the use of other solvents including polyethylene glycol and non-polar solvent.

Fassberg discloses aerosol, formulations for oral or nasal administration, which comprise a medicament, an excipient, propellant and optionally surfactants. The suitable excipients include **alcohols, polyethylene glycols, short chain fatty acids**,

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etc (see page 3). Fassberg discloses that any pharmaceutically active agent which can be delivered by oral or nasal inhalation may be used. Examples include antihistamines, antiallergics, analgesics, antibiotics, steroids, bronchodilators, antihistamines, etc (see page 5, lines 42-50).

Kanios teaches compositions and methods for topical administration of pharmaceutically active agents. Topical administration means a direct contact of the formulation with tissue, such as skin or membrane, particularly the oral or **buccal mucosa** (col. 1, lines 29-59).

Kanios discloses that the composition comprises a therapeutically effective amount of at least one pharmaceutically **active agent**, a pharmaceutically acceptable **solvent** for the active agent (col. 2, lines 22-28). The solvent is preferably a polyhydric alcohol such as polypropylene glycol, ethylene glycol, also solvents including fatty acids such as oleic acid, as well as fatty esters or alcohols. The solvent is present in an amount from about 20 to 50 weight percent based on the total weight of the composition (col. 4, lines 1-49; col. 5, lines 24-66). The concentration of the solubilized active agent can range from **1 to 50%** by weight (col. 8, lines 1-9). The acceptable carrier is intended to be any suitable finite or non-finite carrier including liquids, semi-liquids or solid carriers. Thus the active agent may be admixed with carriers such as spray-solution or any non-finite carrier known in the art for delivery of active agents (col. 8, lines 54-67). Other additives may be incorporated into the formulations such as flavorings (col. 10, lines 48-56).

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Kanios discloses that pharmaceutically active agents suitable for such formulation include galanthamine, lidocaine, mepivacaine, propofol, **testosterone and testosterone cypionate**, atracurium, ipratropium, amantadine, diazepam, pregabalin, primidone, clozapine, chlorpromazine, haloperidol, amitryptiline, buspirone, chlorzoxazone, cyclobenzaprine, interferon beta, estradiol, nimodipine, tacrine, carbidopa, acetylcholine, epinephrine, pergolide, doxepine, clomipramine, zolpidem, amphetamine, dextroamphetamine, methylphenidate, sumatriptan, pemoline, mazindol, desipramine, flumazenil, mesoridazine, etc (columns13-31).

Physicians' Desk Reference teaches a testosterone emulsion or solution for injection for hormone replacement therapy.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of formulations for buccal mucosal administration of Diehl, to have looked in the art for other specific solvents suitable for spray formulations of liquid carriers, as taught by Fassberg et al, with reasonable expectations of successfully preparing suitable formulations for various therapies. Furthermore it is obvious to one of ordinary skill in the art to have substituted any suitable active agent for the analgesics of Diehl's buccal spray formulations as claimed as taught by Kanios et al or Physicians' Desk Reference.

Claims 13-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu et al (WO 9303751) in view of Physicians' Desk Reference.

Fu teaches compositions and methods for the sublingual or buccal administration of therapeutic agents. The compositions comprise a therapeutic agent dissolved or dispersed in a carrier which comprises a solvent, an optional cosolvent, and an oral mucosal membrane transport enhancing agent. The solvent comprises from about 50% w/v to about 95% w/v of the carrier of a non-toxic alcohol. Non-alcohols useful in the said formulations include ethanol, isopropanol, stearyl alcohol, propylene glycol, polyethylene glycol and the like. Most preferred alcohol is ethanol. The cosolvent is selected from water (page 4, lines 12-26). Essential or volatile oils such as peppermint oil, spearmint oil, menthol, etc, are added in a concentration of between about 1 and 5% w/v (page 5, lines 4-10). The said liquid compositions are formulated in a liquid spray or a liquid drop (page 6, lines 1-2). Fu et al, disclosing leuprolide acetate, lacks teachings on testosterone.

Physicians' Desk Reference teaches a testosterone emulsion or solution for injection for hormone replacement therapy.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of formulations for buccal mucosal administration of Fu et al, to have looked in the art for other specific active agents suitable for spray formulations of liquid carriers, as taught by Physicians' Desk Reference, with reasonable expectations of successfully preparing suitable formulations for various therapies. Furthermore it is obvious to one of ordinary skill in the art to have

substituted any suitable active agent for the active agents of Fu et al's buccal spray formulations as taught by Physicians' Desk Reference.

Claims 50 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu et al (WO 9303751) in view of Physicians' Desk Reference as applied to claims 13-29 above, and further in view of Lee et al (6,512,002).

The combined references, discussed above, lack specific disclosure on a method of stimulating erythropoiesis in a patient.

Lee et al discloses methods and pharmaceutical compositions useful in treatment of conditions that are responsive to the elevation of testosterone levels in the body. The said conditions include stimulation of erythropoiesis (see abstract and col. 7, lines 15-36).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have implemented Lee's disclosure of treating various disorders and conditions responsive to testosterone therapy to the disclosure of the combined references with the reasonable expectations of increasing options for patients and health care providers by preparing a safe, easy to use spray formulations.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

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from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,110,486. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are anticipated by the reference claims. In other words, claims 13-29 are generic to all that is recited in claims 1-9 of U.S. Patent No. 6,110,486. Specifically, the buccal spray composition comprising a steroidal hormone, testosterone and a polar solvent recited in claims of instant Application are anticipated by the method of administering the same composition recited in claims of 1-9 of U.S. Patent No. 6,110,486.

Claims 13-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,955,098. Although the conflicting claims are not identical, they are not patentably distinct from

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each other because the instant claims are anticipated by the reference claims. In other words, claims 13-29 are generic to all that is recited in claims 1-18 of U.S. Patent No. 5,955,098. Specifically, the buccal spray composition comprising a steroidal hormone, testosterone and a polar solvent recited in claims of instant Application are anticipated by the compositions and method of administering the same composition recited in claims of 1-18 of U.S. Patent No. 5,955,098.

Claims 13-29 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-34, 54-59 and 80-82 of co-pending Application No. 09/537,118 in view of Physicians' Desk Reference. The double patenting rejection is proper because the examined claims and the reference claims are substantially the same. The difference is that claims of the co-pending Application '118 do not recite testosterone as the active agents. However, Physicians' Desk Reference teaches a testosterone formulation for injection. Thus it would have been obvious to one of ordinary skill in the art to have replaced the active agents of the co-pending Application '118 with the hormone, testosterone as taught by the Physicians' Desk Reference to provide a new dosage form and a new option for treating patients.

This is a provisional obviousness-type double patenting rejection.

Pertinent Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

1) Oguri et al (JP 02-026661) teaches formulations for aerosol delivery comprising an active agent and a liquid carrier. Suitable active agents include analgesics and carrier formulations include polar and non-polar solvents and other agents. Carrier formulations may comprise a mixture of a polar and a non-polar solvent. Polar solvents include water, alcohols such as ethyl alcohol, propylene glycols. Non-polar solvents include hydrocarbons or halogenated hydrocarbons are suitable. Menthol is one of flavors used.

2) Kim (6,143,329) teaches aqueous-based pharmaceutical compositions comprising an active agent such as triamcinolone, purified water, Polysorbate and dextrose (see example 1). The said formulations are placed in a spray bottle for delivery to the surface of mucosa.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mina Haghighatian
May 24, 2006



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